AMENDMENTS TO THE SPECIFICATION

Please replace the Title with the following amended Title:

METHOD OF IDENTIFYING A COMPOUND THAT MODULATES BINDING OF SERUM AMYLOID A (SAA) TO A FRPL1 RECEPTOR

Please replace the Brief Description of the Drawings with the following amended Brief Description of the Drawings:

BRIEF DESCRIPTION OF THE DRAWINGS

FIGURE 1A-C Cross-desensitization of Ca^{2+} mobilization in human monocytes between SAA and fMLP. Fura-2 loaded monocytes were sequentially stimulated with SAA and fMLP (panel A) or vice versa (panel B and C), and the ratio of fluorescence at 340 and 380 nm wavelength was recorded and calculated with the FLWinLab program.

FIGURES 2A-F ~~2A-2E~~ Calcium mobilization in FPRL1 transfected HEK 293 cells. FPRL1/293 cells were loaded with Fura-2 and were stimulated with various concentrations of fMLP (FIGURE 2A) or SAA (FIGURE 2B). SAA does not induce Ca^{2+} mobilization in FPR expressing 293 cells or mock transfected 293 cells (FIGURES 2C-2D). FIGURES 2E-2F show ~~FIGURE 2E shows~~ the sequential stimulation of FPRL1/293 cells with SAA and fMLP or vice versa.

FIGURES 3A-C ~~3A-3C~~ Chemotactic activity of SAA for human monocytes and cells transfected to express chemoattractant receptors. Different concentrations of SAA were placed in the lower wells of the chemotaxis chamber. Monocytes, FPRL1/293 cells or FPR expressing ETFR cells were placed in the upper wells. After incubation, the cells migrated across the polycarbonate filter were counted and photographed; SAA 0.8 :M, fMLP 100 nM. The cell migration was expressed as chemotaxis index representing the fold increase of the cells migrating in response to stimulants over control medium. FIGURE 3A: migration of FPRL1/293 cells in response to SAA and fMLP. FIGURE 3B: migration of FPR expressing ETFR cells in response to SAA and fMLP. FIGURE 3C: effect of HDL on SAA induced FPRL1/293 cell migration. HDL at 1000 :g/ml mixed with 0.8 :M SAA was preincubated at 37°C for 4 h. The mixture was

then tested for chemotactic activity on FPRL1/293 cells. The HDL/SAA mixture without preincubation was also tested for chemotactic activity and yielded similar results.

FIGURE 4A-D Binding of ^{125}I-SAA to human monocytes and FPRL1/293 cells. rhSAA was radio-iodinated by the chloramine T method and the binding of ^{125}I-SAA to FPRL1/293 cells (panel A) or monocytes (panel B) was measured by adding a constant concentration of ^{125}I-SAA to the cells in the presence of increasing concentrations of unlabeled SAA. The data was analyzed and plotted using LIGAND software on a Macintosh computer. Panel C shows the displacement of ^{125}I-SAA binding on monocytes by unlabeled SAA and fMLP. Same results were obtained with FPLR1/293 cells (panel D).

Please replace the paragraph at 10:7-16 with the following amended paragraph:

Further, rhSAA induced Ca^{2+} mobilization in cells transfected with FPRL1 (FPRL1/293 cells) (FIGURE 2B), but not in FPR expressing cells or mock transfected 293 cells (FIGURE 2C, D). The EC50 of rhSAA on FPRL1 transfected cells was 250 nM, suggesting that SAA activates FPRL1 with higher efficacy than fMLP. This was supported by studies of cross-desensitization of Ca^{2+} flux between SAA and fMLP in FPRL1/293 cells. As shown in FIGURES 2E, F ~~FIGURE 2E~~, although sequential stimulation of FPRL1/293 cells with SAA and fMLP resulted in bidirectional desensitization, SAA was able to desensitize the cell response to a 100 fold excess of fMLP. In contrast, fMLP at 100 fold excess of SAA, only partially desensitized the effect of SAA ~~(FIGURE 2E)~~.

Please replace the paragraph at 52:27-53:12 with the following amended paragraph (to excise improper characters which are not reproduced below):

Various types of antisense oligonucleotides complementary to the *SAA or FPRL1* mRNA can be used. In one preferred embodiment, stable and semi-stable antisense oligonucleotides described in International Application No. PCT WO94/23026, hereby incorporated by reference, are used. In these molecules, the 3 prime end or both the 3 and 5 prime ends are engaged in intramolecular hydrogen bonding between complementary base pairs. These molecules are better able to withstand exonuclease attacks and exhibit increased stability compared to conventional antisense oligonucleotides. In another preferred embodiment, the antisense oligodeoxynucleotides

described in International Application No. WO 95/04141 are used. In yet another preferred embodiment, the covalently cross-linked antisense oligonucleotides described in International Application No. WO 96/31523 are used. These double- or single-stranded oligonucleotides comprise one or more, respectively, inter- or intra-oligonucleotide covalent cross-linkages, wherein the linkage consists of an amide bond between a primary amine group of one strand and a carboxyl group of the other strand or of the same strand, respectively, the primary amine group being directly substituted in the 2' position of the strand nucleotide monosaccharide ring, and the carboxyl group being carried by an aliphatic spacer group substituted on a nucleotide or nucleotide analog of the other strand or the same strand, respectively.

Please replace the paragraph at 61:32-62:20 with the following amended paragraph (to excise embedded hyperlinks which are not reproduced below):

By using this computational protocol, genome sequence data bases such as maintained by various organizations including: tigr.org/tdb, genetics.wisc.edu, stanford.edu/~ball, hiv-web.lanl.gov, ncbi.nlm.nih.gov, ebi.ac.uk, patteur.fr/other/biology, and genome.wi.mit.edu, can be rapidly screened for specific protein active sites and for identification of the residues at those active sites that resemble a desired molecule. Several other groups have developed databases of short sequence patterns or motifs designed to identify a given function or activity of a protein. Many of these databases, notably Prosite (expasy.hcuge.ch/sprot/prosite), Blocks (blocks.fhcrc.org), and Prints (biochem.ucl.ac.uk/bsm/dbfrowser/PRINTS/PRINTS), the Molecular Modelling Database (MMDB), and the Protein Data Bank can use short stretches of sequence information to identify sequence patterns that are specific for a given function; thus they avoid the problems arising from the necessity of matching entire sequences. In this manner, new modulating agents are rationally selected for further identification by SAA/FPRL1 characterization assays, as described above. Rounds or cycles of functional assays on the molecules and derivatives thereof and further FFF refinement and database searching allows an investigator to more narrowly define classes of modulating agents that produce a desired effect on assembly of the SAA/FPRL1 complex and/or SAA/FPRL1-mediated signal transduction.

Please replace the paragraph at 72:24-73:23 with the following amended paragraph (to excise extraneous characters which are not reproduced below):

Recombinant human (rh) SAA was purchased from Pepro Tech Inc. (Rocky Hill, NJ) with the sequence as follows:
MRSFFSFLGEAFDGARDMWRAYSDMREANYIGSDKYFHARGNYDAAKRGPGGVWAA EAISNARENIQRFFGRGAEDSLADQAANEWGRSGKDPNHFRPAGLPEKY. (SEQ. ID. No. 1). This rhSAA corresponds to SAA-1α, one of the major SAA isoforms in the serum, except for the addition of a methionine at the NH2 terminus as well as the substitution of aspartic acid for asparagine at position 60, which appears in the SAA2 isoform (reviewed in ref. Steinkasserer et al., Biochem. J., 268:187-193 (1990)). rhSAA at concentrations used in the study was negative for endotoxin as assessed by Limulus amebocyte lysate assays (sensitivity: 0.06 IU/ml. BioWhittaker, Walkersville, MD). High density lipoprotein (HDL) was purchased from Sigma (St. Louis, MO). Human peripheral blood enriched in mononuclear cells or neutrophils was obtained from normal donors by leukapheresis (courtesy of Transfusion Medicine Department, Clinical Center, National Institutes of Health, Bethesda, MD). The blood was centrifuged through Ficoll-Hypaque (Sigma) and mononuclear cells (PBMC) collected at the interphase were washed with PBS and centrifuged through a 46% isoosmotic Percoll (Pharmacia, Uppsala, Sweden) gradient followed by elutriation to yield monocytes (purity: >90%). Neutrophils were purified by 3% dextran/PBS sedimentation as described elsewhere (Badolato et al., J. Exp. Med., 180:203-209 (1994)) and were more than 98% pure. The cells were resuspended in RPMI 1640 medium containing 10% FCS (Hyclone, Logan, UT) for future use. The molecular cloning of the receptors for fMLP was described previously (Murphy et al., *J. Biol. Chem.,* 267:7637-7643 (1992); Gao, J.L. and P.M. Murphy, *J. Biol. Chem.,* 268:25395-25401 (1993); Murphy, P.M. and D. McDermott, *J. Biol. Chem.,* 266:12560-12567 (1991); and Ali et al., *J. Biol. Chem.,* 273:11012-11016 (1998)). The cDNAs encoding classical formyl peptide receptor FPR and its variant FPRL1 were stably transfected into human embryonic kidney epithelial cell line 293 that were cultured in DMEM in the presence of 800 :g/ml geneticin (G418, GibcoBRL, Grand Island, NY) to maintain selection. A rat basophil leukemia cell line stably transfected with FPR (ETFR cells) was also used in the study (a kind gift from Drs. H. Ali and R. Snyderman, Duke University Medical Center, NC).